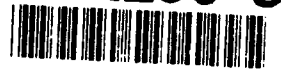

INVESTIGATIONS OF HEMORRHAGIC FEVER WITH RENAL SYNDROME (HFRS) IN YUGOSLAVIA

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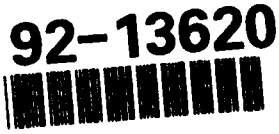

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Five hundred and forty-four rodents and small mammals were trapped in various regions of Yugoslavia and examined. Antihantaviruses, immunofluorescent (IF) antibodies were detected in the blood samples of 129 animals. Antigens were detected in the lung samples of 139 animals. Sixty-seven animals tested positive for both the presence of antibodies in the sera and antigens in the lungs. Hantaviral antibodies and/or antigens were detected most in the yellow-necked mouse (Apodemus flavicollis) (88/189), the wood mouse (Apodemus sylvaticus (28/146), the striped field mouse (Apodemus agrarius) (10/64), house mouse (Mus musculus) (14/29), and the Norway rat (Rattus norvegicus) (14/21). Five other species of rodents and insectivora were infrequently infected. Hantavirus infection in small mammals, according to age, gender, location and species indicated a disparity from region to region prior to and during the epidemic.

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Studies on the immune status of healthy people in various HFRS endemic areas were conducted. Blood samples from over 761 forest workers, farmers, and other individuals with considerable outdoor exposure were collected and tested serologically for antibodies to hantaviruses. The 130 individuals possessed hantaviral antibodies. A nationwide epidemic of hemorrhagic fever with renal syndrome (HFRS) occurred in Yugoslavia in 1989. From 609 of HFRS suspected individuals we were able to obtain 872 sera samples. Six hundred and nine individuals were hospitalized and 15 deaths occurred. The epidemic occurred in all six republics and two provinces of Yugoslavia, in both previously recognized and newly recognized foci areas. Of the 226 patients with serologically confirmed HFRS, 182 resided in Bosnia and Hercegovina or in Serbia. The severity of disease differed from region to region, with an overall fatality of 6.6% (15/226). Patients from southern Yugoslavia tended to have more severe disease and exhibited two types of antibody patterns, while approximately equal numbers of clinically severe and mild cases of HFRS were registered in central Yugoslavia, where four types of antibody patterns were found. Two of these antibody patterns suggested the existence of hantaviruses which are antigenically distinct from those reported to date. In the beginning of the epidemic, it was determined that the most severe cases of HFRS, and ultimately the highest lethality rate, occurred in those individuals with a specific immune response against Hantaan rather than the Puumala.

FOREWORD

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Ana Glisic, Februat 26, 1992.
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INTRODUCTION

Hemorrhagic fever with renal syndrome (HFRS), an acute viral nephropathy characterized by high fever, headache, abdominal and back pain, hemorrhagic manifestation and renal insufficiency, is widespread across the Euroasian landmass (1). Clinically severe HFRS, caused by Hantaan virus, occurs in Korea, the People's Republic of China and far eastern U.S.S.R., as well as in eastern Europe, including the Balcan countries, where mortality is as high as 15% (2-7). HFRS in other European countries, Scandinavia and European U.S.S.R. takes a much milder clinical form, with mortality of less than 1%, and is caused by Puumala virus (8-12). Hantaan and Puumala viruses are members of the Hantavirus genus, which also includes Seoul and Prospect Hill viruses (13,14). Very recently, the investigators et al. reported a close etiologic relation between HFRS in Korea, China, Japan and European countries (13,14,15). Multiple species of arvicolid and murid rodents serve as the natural reservoirs of hantaviruses, and humans are primarily infected by the respiratory route (1).

The etiological agent of HFRS in Korea (Korean hemorrhagic fever-KHF) was named as Hantaan virus for the Hantaan river that runs along the 38th parallel during the Korean war when 2,422 U.S. soldiers were hospitalized with this disease. The immunofluorescent and another technique made it possible to study some characteristics of the virus and an examination of the dynamics of transmission of the virus among different species of small mammals and insectivora (12).

Very recently, the investigator et al. reported a close etiologic reaction between Korean hemorrhagic fever in Korea and HFRS in Europe, Asia and Japan (12-15,17). At least six antigenically related but distinct viruses, belonging to the newly defined Hantavirus genus of the family Bunyaviridae, have now been recognized (4,13,14,16,21).

Since 1952 when the first case of HFRS was reported in Bosnia and Herzegovina and Slovenia (22), epidemics and sporadic cases of clinically mild and severe HFRS have been recorded annually throughout Yugoslavia (2,5,6,10,11,18,26), with so far more than 1,000 cases, with mortality rates exceeding 10% in some regions (16-22). In the republic of Montenegro, the first cases were recognized in 1967 and in the Serbia-region of Cacak in 1979 (2,6). In 1961 the first recognized epidemic of HFRS occurred in a military camp in the forest Fruska Gora in Vojvodina province, 50 km west of Belgrade. A total of 46 soldiers were ill (13 with severe and 33 with mild disease) with one fatality (11). A second epidemic in 1967, affecting more than 200 individuals with

five fatalities, centered in Bosnia and Herzegovina (Fojnica), Croatia (Plitvice Lakes) and Montenegro (5,26). Nineteen years later, in 1986, an outbreak of HFRS occurred in all six republics and two provinces of Yugoslavia (10). Studies conducted two years prior to this last outbreak resulted in the isolation of two antigenically and biologically distinct hantaviruses, named Fojnica and Vranica, from the yellow-necked mouse (Apodemus flavicollis) and the bank vole (Clethrionomys glareolus), respectively (9). The demonstration of these viruses, which closely resemble Hantaan and Puumala viruses, was consistent with the serologic data reported previously (8,15,17) and with the clinical observation of both severe and mild forms of HFRS in Yugoslavia (2,5,6,10,11,18,22,26). However, some patients with HFRS exibited atypical serological responses to prototype hanatviruses strains, as well as to virus strains Fojnica and Vranica, suggesting the existence of other antaviruses variants in Yugoslavia (3,9). A major outbreak of HFRS occurring in 1989 in Yugoslavia, which centered in Bosnia and Herzegovina (near Sarajevo) and in Croatia and Serbia, offer us an excellent opportunity to investigate various aspects of this important disease.

This report presents the results of the project on:

1. Characterization of HFRS in Yugoslavia
2. Animal reservoir of virus nature

MATERIALS AND METHODS

A major outbreak of HFRS occurring in 1989 in Yugoslavia, which centered in Bosnia and Herzegovina (near Sarajevo) and in Croatia (near Zagreb) and widely in Serbia, offered us an excellent opportunity to investigate various aspects of HFRS - this important disease. We reported on the lessons learned about the epizootology and epidemiology of HFRS before, during and after this epidemic.

Patient population

A nationwide epidemic of HFRS occurred in Yugoslavia from January to December 1989. Eight-hundred seventy-two sera from 609 hospitalized patients suspected of having HFRS were referred to us for testing at the National Reference Laboratory for Viral Hemorrhagic Fever in Belgrade. Signs and symptoms included sudden onset of high fever, abdominal or back pain, retroorbital headache, vomiting, hemorrhagic manifestations (such as scleral hemorrhages, epistaxis, hemoptysis, ecchymoses), prolonged clotting time, proteinuria and/or oliguria. Patients from hospitals in all six Republics (Bosnia and Herzegovina, Croatia, Macedonia, Montenegro, Serbia, Slovenia and two Provinces (Kosovo and Vojvodina) were studied.

Healthy people

Blood samples from 761 forest workers, farmers and other individuals with considerable outdoor exposure were collected during the period of investigation and tested serologically for antibodies to Hantaviruses (Hantaan 76-118 and Puumala-Hallnas B1).

Trapping and testing of small mammals

Small mammals were captured using live traps between October 1988 and October 1989 in foci known to be endemic for HFRS, including Ivanjica, Cacak and Pozarevac and surrounding regions in Serbia, Novo Mesto in Slovenia, and Karlovac and Plitvice Lakes in Croatia. In addition, animals were trapped in newly recognized HFRS foci, namely Hadzici and Olovo in Bosnia and Herzegovina (which formed the center of the epidemic in 1989). The 544 small mammals were trapped around houses and fields and forests near the homes of HFRS patients, except in the Plitvice Lakes region, where animals were trapped only in the forest. Animals were speciated in the field laboratory. Sera, collected from 516 small mammals, were diluted 1:16 in phosphate buffered

saline (PBS, pH 7.2) and stored at -20 C until testing for anti-hantaviral antibodies. Lung tissues were removed aseptically from 541 animals and stored in liquid nitrogen, prior to being examined for hantaviral antigen by the indirect immunofluorescent antibody (IFA) technique (9), using convalescent-phase sera from a Korean patient with serologically confirmed Koean hemorrhagic fever, a Swedish patient with serologically confirmed nephropathia epidemica, and two Yugoslavian HFRS patients (one with mild disease and the other with severe disease), and 8 antiglobulin units of fluorescein isothiocyanate-conjugated goat antibodies to human immunoglobulins (INEP Laboratory, Belgrade). Sera from seronegative individuals served as negative controls.

Serological methods

Sera from 609 patients with suspected HFRS and from 516 small mammals (predominantly rodents) were tested for antibodies against Hantaan virus strain 76-118 (12) and Puumala virus strain Hallnas (27) by the IFA method, using fluorescein isothiocyanate-labeled goat antibodies to human and mouse immunoglobulins. Human sera were also tested for antibodies against Fojnica (9), Vranica (9), Seoul (13,17) and Prospect Hill viruses (16). Sera were initially tested at a 1:32 dilution using spot slides of Vero E6 cells infected with hantaviruses as described previously (9,17). Sera showing characteristic intracytoplasmic, virus-specific fluorescence were considered positive and were diluted further in two-fold increments. IFA titers were expressed as the reciprocal of the highest dilution of serum giving typical fluorescence. Human and mouse sera lacking antibodies to hantaviruses and uninfected Vero E6 cells were included as negative controls.

Human sera were also tested for IgM antibodies to Hantaan and Puumala viruses by ELISA (19). Briefly, two-fold dilutions beginning at 1:100) of each serum were added to wells coated with affinity purified goat anti-human IgM (u chain-specific) for 1 hr at 37 C. Anti-Hantaan or anti-Puumala virus-specific IgM antibodies were then detected in virus or control antigen and antivirus-specific rabbit antibodies, which were detected by peroxidase-labeled anti-rabbit IgG.

RESULTS

Studies of HFRS Patients in 1989

From 609 patients with signs and symptoms suggestive of HFRS (sudden onset, abdominal or back pain, headache, vomiting, epistaxis, excessive menstrual bleeding, and slow clotting time, proteinuria, hematuria, anuria, oliguria, hemorrhagic manifestation), 226 were found to have serological evidence of acute hantavirus infection with lethality of 6.6% (Table 1).

The majority of HFRS patients were from Bosnia and Hercegovina (108 patients) or from Serbia including Kosovo and Vojvodina (74 patients) (Fig. 1 and Table 1). Distribution and location of HFRS are shown in Figure 2. Hemorrhagic fever and hemorrhagic fever with acute renal insufficiency (beside another 14 diagnosis) were the tentative diagnoses in 66 and 46, respectively, of the 226 serologically confirmed cases at the time their sera were referred to the National Reference Laboratory in Belgrade. Immune response to Hantaan and Puumala-hantaviruses according to diagnosis were done in Table 2.

Notably, serological confirmation was most common in patients from Bosnia and Hercegovina and from Croatia (Table 1). Among the 383 patients in whom anti-hantaviral antibodies were not detected, fever of unknown origin, acute renal disease and suspected hemorrhagic fever were the most frequent diagnosis.

Clinical disease among the serologically confirmed cases of HFRS varied from mild to severe, and the severity of disease was different from foci to foci. In Croatia and Slovenia the mild form of disease predominated. By contrast, patients from Macedonia and Serbia (including Kosovo and Vojvodina) had more severe HFRS (fatality, 16.3%), while in central Yugoslavia (Bosnia and Hercegovina), approximately equal numbers of clinically severe and mild disease were registered, with a fatality of 5.5% (Table 1).

Depending on immune response to Hantaan and Puumala antigens along the application of two serological methods (IFA and ELISA), patients were classified into four groups. Of the 226 HFRS patients, 135 reacted primarily to Hantaan or Hantaan-like viruses (group I and II), while 91 reacted principally to Puumala or Puumala-like viruses (group III and IV). Patients in group I, like HFRS patients in Korea and China, possessed high antibody titers to Hantaan and Seoul viruses with much lower reactivity to Puumala and Prospect Hill viruses by IFA and ELISA (patients 1

and 2 in Table 3). Patients in group II had high antibody titers to Hantaan, Seoul and Puumala viruses by IFA with high IgM antibody titers to Hantaan virus by ELISA and without IgM reactivity to Puumala virus by ELISA (patients 3 to 5 in Table 3). Clinical disease among patients in these groups tended to be severe. Of the 15 fatal cases, 14 belonged to groups I and II for an overall mortality of 10.4. From the blood and urine of the patient from group II, who died, hantavirus has been isolated in tissue culture Vero-E6 cells.

Patients in group III, like Scandinavian patients with nephropathia epidemica, had high antibody titers to Puumala virus by IFA and ELISA and lower antibody titers to Hantaan, Seoul and Prospect Hill viruses by IFA and ELISA (patients 6 and 7 in Table 3). Finally, patients in group IV appeared to be infected with a virus which was antigenically distinct from Puumala virus, as evidenced by their striking reactivity to Puumala virus by IFA and ELISA in the absence of reactivity to Hantaan virus by either IFA or ELISA (patients 8 to 10 in Table 3). Disease among patients in these groups tended to be clinically mild, resembling a flu-like illness, but some patients had more severe disease, with one ending in death (mortality in this group, 1%).

All four groups of antibody responses were found in patients from Bosnia and Hercegovina and from Serbia (Ivanjica, Cacak), while patients from southeast Serbia, Kosovo, Vojvodina, and Macedonia exhibited group II type responses, indicating infection with a new hantavirus serotype. Group III type responses were found primarily in patients from Croatia and Slovenia, indicating infection with the Puumala serotype.

Of the 138 HFRS patients (108 males and 30 females whose occupations were known, 31 were farmers, 21 were soldiers, 18 were forestry workers, 20 were students, and 18 were homemakers. The remaining 30 had a variety of other vocations (Table 4). Overall, five of the 15 fatal cases were women, all of whom were homemakers. Ages were available for 177 of the 226 HFRS patients, and of these, 112 (63%) were between the ages of 21 and 50 years. Four patients (2%) were younger than 10 years, 14 (8%) were between 11 to 15 years, 18 (10%) were between 16 and 20 years and 29 (16%) were 51 years or older (Table 5).

The seasonal occurrence of HFRS indicated two peaks. One peak during the summer and the other in late autumn (Figure 3). The peak in autumn was associated with disease due to the Puumala serotype, while the late summer peak was due primarily to the Hantaan serotype.

Immune status of healthy people from HFRS endemic areas

Studies on the immune status of healthy people in various HFRS endemic areas were conducted before, and during the 1989 epidemic. Blood samples from 761 forest workers, farmers and other individuals with considerable outdoor exposure were collected and tested serologically for antibodies against Hantaan and Puumala viruses by IFA test. The 130 individuals possessed hantavirus antibodies to Hantaan or Puumala or both viruses. Hantaviruses antibodies were found in different percentage (Tables 6, 7, 8). Most of the attached were people professionally connected with the field work (farmers) and then follows the others. These results were found in people from Ivanjica, the center of HFRS epidemic in 1986 (Serbia). In sera from Hadzici, the center of the epidemic in 1989, the results have shown that the greater percentage from positive persons have antibodies of Hantaan (77.7%) in comparison with results to Puumala (16.6%), while for both viruses, the percentage is not so high (5.5%). Similar but not identical results were in the Olovo location, center of the epidemic too (Table 8).

Small mammals survey

Of the 554 small mammals captured in the different foci, 526 were wild rodents belonging to 9 species and 19 were insectivores belonging to 4 species (Table 9). Anti-hantaan antibodies were detected by IFA in 129 of the 516 animals from whom sera were available, and hantaviral antigen was found in lung tissues from 139 of the 541 small mammals belonging to 11 species (Table 9). The yellow-necked mouse (Apopdemus flavicollis) was the most frequently infected rodent species in Serbia (Ivanjica) and in Bosnia and Hercegovina (Olovo and Hadzici), which formed the centers of the epidemic in 1989. In Olovo and Hadzici (central part of Yugoslavia) where more than 100 cases of HFRS occurred, four of five rodent species captured during the peak of the epidemic in July 1989 were infected with hantaviruses (Table 9 and 10).

In Cacak, Ivanjica, Pozarevac (Serbia) and in Olovo (Bosnia and Hercegovina), the wood mouse (Apodemus sylvaticus) was commonly infected, while virus-infected striped mice (Apodemus agrarius) were found only in Cacak and Pozarevac (Central part of Serbia) (Table 9).

In the Plitvice Lakes region (Croatia), numerous infected populations of the bank vole (Clethrionomys glareolus) and Apodemus flavicollis were captured, but only one HFRS case was registered in 1989. Of significance was the conspicuous absence of Apodemus sylvaticus. Interestingly, a high percentage of

virus-infected house mice (Mus musculus) were captured in Pozarevan and Ivanjica (Serbia), and infected Norway rats (Rattus norvegicus) confirmed urban cases of HFRS have been reported.

Hantavirus infection in small mammals according to age, gender and location indicated a disparity from region to region prior to and during the epidemic (Table 11 to 27). Female animals were over represented before the epidemic and juvenile and subadult forms were under represented during the epidemic (Olovo, Hadzici) (Table 12).

DISCUSSION

Using four hantavirus serotypes (Hantaan, Seoul, Puumala and Prospect Hill) and two serological methods (IFA and ELISA), we gained important insights into the epidemiology and epizootology of HFRS in Yugoslavia. Unlike the HFRS in 1986 in which most patients originated in Montenegro, the outbreak in 1989 centered primarily in Bosnia and Hercegovina and in Serbia, with only one confirmed case in Montenegro. Earlier serologic studies indicated the existence of at least two hantavirus serotypes in Yugoslavia (15,17). The subsequent isolation of Fonjnica and Vranica viruses, which were antigenically indistinguishable from Hantaan and Puumala viruses, respectively, was consistent with the serologic data and clinical observations (9). However, some HFRS patients from Yugoslavia exhibited sero reactivities which were distinct from individuals infected with Hantaan (or Fojnica) and Puumala (or Vranica) viruses (9). Similarly, in the present study, the immune response of some HFRS patients to Hantaan, Seoul, Puumala and Prospect Hill viruses indicated the other, as yet identified serotypes or variant of hantaviruses may circulate in Yugoslavia. On the basis of serological results, Hantaan and Hantaan-like viruses circulate primarily in south and central Yugoslavia, while Puumala and Puumala-like viruses abound principally in the northern and central sectors. The characterization of antigenically distinct hantaviruses, newly isolated from blood and urine of HFRS patients, now in progress, may clarify the spectrum of disease-causing hantaviruses in Yugoslavia.

The seasonal distribution of HFRS in Yugoslavia with culmintion in July and August, is similar to that in Hungary and Bulgaria (25) and in Greece (1). By contrast, in Scandinavia and Far East Asia, HFRS occurs most often during the spring and late autumn (20,24). The summer peak can be accounted for by infection among children, who were exposed to excreta of virus-infected rodents during their summer holidays spent in special mountain houses (bacije) or while caring for cattle or picking wild berries or mushrooms in the forests.

Since the first outbreak of HFRS in Yugoslavia in 1961, rodents have been known to play an important role in the enzootic cycle of the disease. Multiple species of rodents and other small mammals in Yugoslavia have been previously identified to be naturally infected with hantaviruses (8,10). In addition to these species, the present study found evidence of hantavirus infection in two other species. However, it is not known whether all of these species serve as reservoirs for human infection, or

which species merely serve as accessory hosts, participating only in the maintenance of the enzootic cycle. Also, the presence of infection in multiple species of rodents and insectivores makes problematic precise identification of the species responsible for any given epidemic. The more widespread geographic distribution of hantaviruses among rodents than the distribution of HFRS in Yugoslavia may be due to the existence of less pathogenic hantaviruses, such as Prospect Hill virus (16,28), or the absence of contact between particular rodent species and humans.

It is evident from age-specific prevalences of hantavirus infection among small mammals that the high populations of adult rather than subadult or juvenile animals are associated with epidemic disease. At the same time, the greater proportion of male animals in Hadzici (66.7%) and Olovo (71.4%) would predict a decline in population and subsequent decrease in HFRS cases. This has been confirmed in 1990, when only a few sporadic cases of HFRS have been reported in Bosnia and Hercegovina.

To what extent hantavirus infection directly or indirectly influence the population cycles of rodents and other small mammals in HFRS-endemic foci is unknown. In addition, the complex interaction between climate, rodents and insectivore populations and human activities involved in the genesis of HFRS epidemics in the exact same regions (for example in 1967 and 1986 in Montenegro and in 1967 and 1989 in Bosnia and Hercegovina) are not well understood. However, some insights were gained from the study of Plitvice Lakes region in Croatia, which appears to fulfill the epizootiologic conditions for the appearance of an epidemic. Specifically, the high population density of rodents of adult age and high percentage of hantavirus-infected Apodemus flavicollis and Clethrionomys glareolus are in keeping with features during epidemic years. However, epidemic disease did not occur in the Plitvice Lakes region in 1989. The possible explanations for this include the following: Plitvice Lakes has been proclaimed a National Park; the local population, which enjoys a high standard of living, is primarily occupied with tourism; movement through the park area is restricted to asphalt paths; the collection of forest fruits and flowers is strictly prohibited. So while the potential exists for epidemic disease, various circumstances and preventive measures have reduced the risk of infection.

High prevalence of hantavirus infection among peridomestic rodents (Mus musculus and Rattus norvegicus) indicate their possible role in maintenance of the epizootic cycle, as well as their importance for infection in humans (7,32). Since murid, cricetid and arvicolid rodent species are sympatric and synchronistic in some habitats, the possibility exists for

genetic reassortment among hantaviruses, but definitive data are lacking.

HFRS has become an emergent problem of immense public health concern in several geographic regions, where invasion of rodent habitats for the purpose of agricultural or industrial development, or as a consequence of recreational activities, has produced potential for epidemic disease. The apparent circulation of more than two major disease-causing hantavirus serotypes in Yugoslavia, and the multiple infected animal species makes for an extraordinary challenge for prevention and control. Further investigations are necessary to delineate the myriad ecologic, zoologic, sociologic, clinicopathologic and virologic aspect of HFRS in Yugoslavia.

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TABLE 1.

HFRS IN YUGOSLAVIA IN 1989 *

Republics and Provinces	No. clinically suspected HFRS	No. serologically positive	% positive	Lethality	%
SR BOSNIA AND HERZEGOVINA	226	108	40,6	6	5,5
SR CROATIA	47	27	57,5	-	-
SR MACEDONIA	15	6	40,0	-	-
SR MONTENEGRO	4	1	25,0	-	-
SR SLOVENIA	-	10	-	-	-
SR SERBIA	179	43	24,0	7	16,3
a) KOSOVO	83	29	28,6	2	6,9
b) VOJVODINA	15	2	13,3	-	-
TOTAL	609	226	37,1	15	6,6

*These data were formed on the base of serologically examined sera in National Reference Laboratory for viral hemorrhagic fever in Belgrade, using immunofluorescent test and ELISA IgM test with Hantaan and Puumala antigens.

Figure 1.

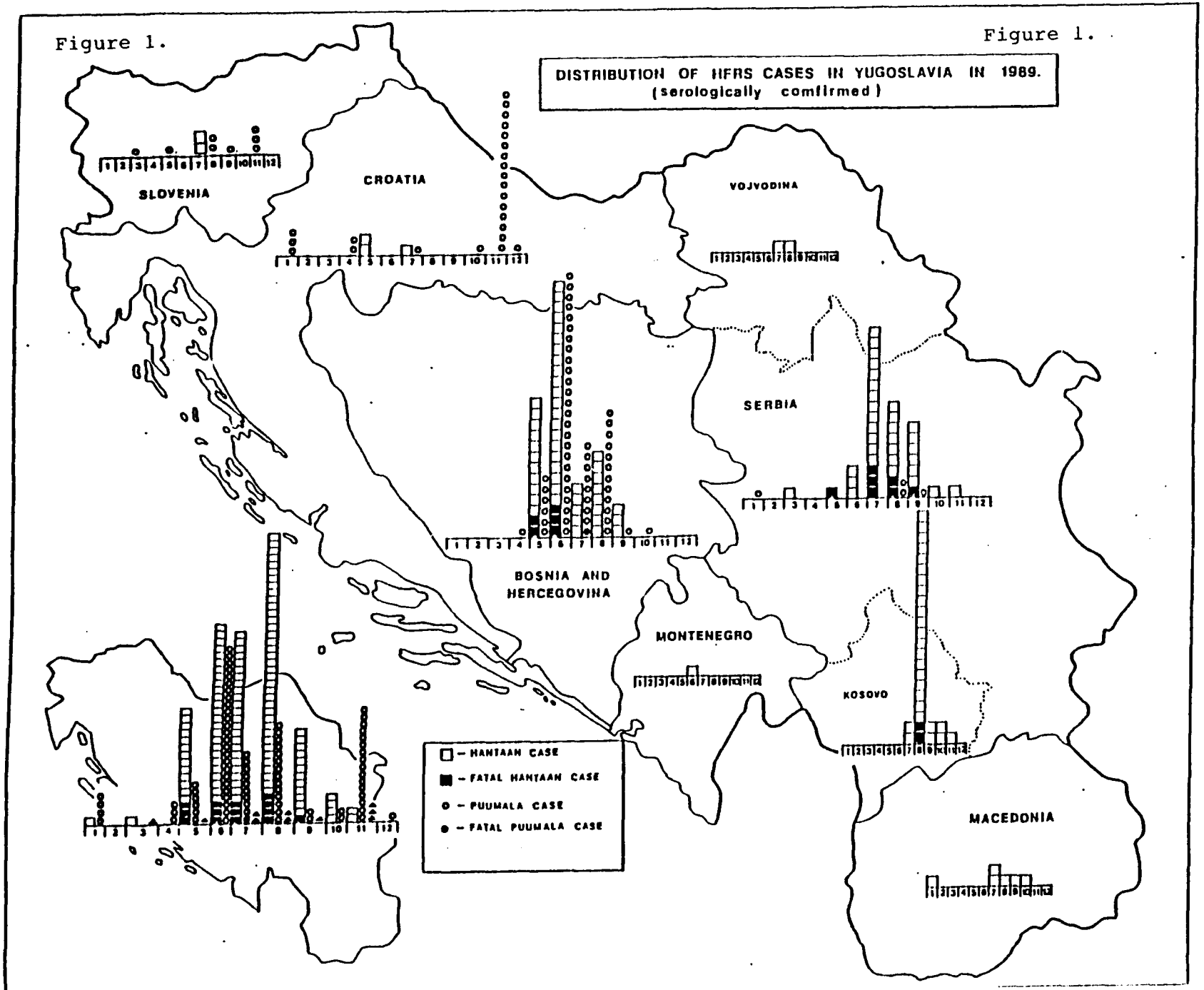

Figure 1.

Teble 2.

PRELIMINARY DIAGNOSIS	IMMUNE RESPONSE TO: HTN	NE
Febris hemorrhagica	51	15
Status febrilis	14	46
Febris hemorrhagica, Insufficientio renum acuta	33	13
Status febrilis, Bronchopneumonia	-	11
Insufficientio renum acuta, Gastroenterocollitis acuta	10	-
Abdomen acuta	6	-
Febris hemorrhagica suspecta Encephalitis acuta	6	-
Febris hemorrhagica suspecta Meningoencephalitis ac.	3	-
Glomerulonephritis acuta, Insufficientio renum acuta	3	1
Insufficientio renum acuta	3	-
Enteritis acuta	2	-
Intoxicatio alimentare, Azotemia extrarenalis	2	1
Tonsilopharingitis acuta	-	2
Nephritis acuta	-	2
Insufficientio remum acuta, Gastritis erosiva	1	-
Botulism in ops.	1	-
	135	91

Figure 2.

Distribution of Serologically Confirmed Cases of HFRS in Yugoslavia in 1989

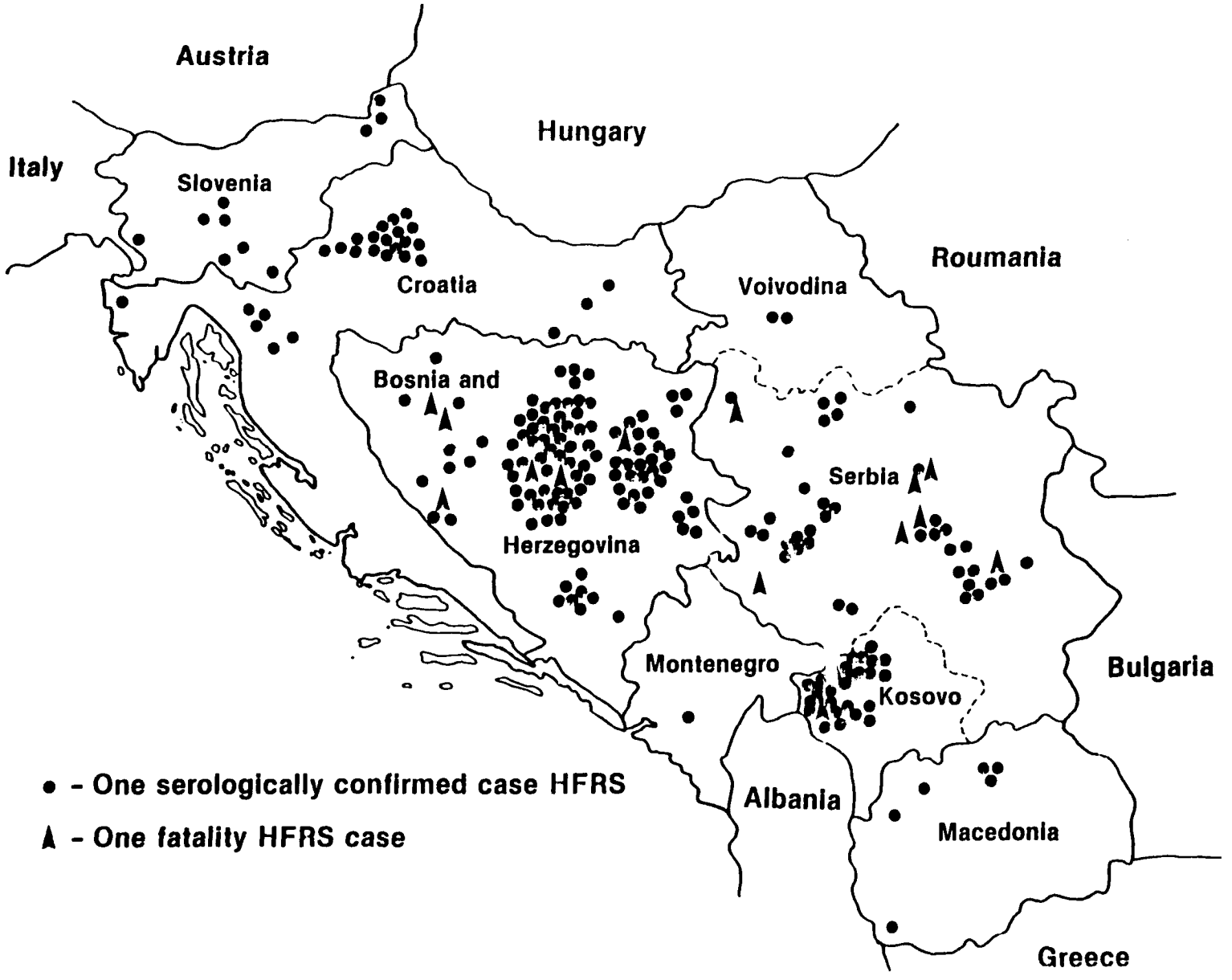

Table 3.

Table 2. Seroreactivity of representative patients with hemorrhagic fever with renal syndrome to Hantaan and Puumala viruses by the indirect immunofluorescent antibody (IFA) test and by enzyme immunoassay (ELISA).*

		IFA				ELISA IgM	
Group	Patient	Hantaan	Seoul	Puumala	Prospect Hill	Hantaan	Puumala
I	1	>2048	2048	128	<16	3200	800
	2	>2048	2048	256	16	12800	400
II	3	1024	1024	1024	16	3200	<100
	4	1024	1024	1024	16	6400	<100
	5	>2048	1024	>2048	128	>12800	<100
III	6	256	1024	1024	32	1600	>12800
	7	128	64	512	64	400	3200
IV	8	<16	<16	2048	64	<100	>12800
	9	16	16	>2048	256	<100	>12800
	10	<16	<16	2048	64	<100	>12800

*Antibody titers were determined against hantaviruses on serum samples obtained between 7 and 10 days after onset of illness. Antibody titers against Fojnica and Vranica viruses were similar to those against Hantaan and Puumala viruses, respectively.

Table 4. OCCUPATION AND SEX OF HFRS CASES IN YUGOSLAVIA DURING EPIDEMIC IN 1989

Location / Occupation		Bosnia and Hercegovina	Croatia	Macedonia	Montenegro	Serbia	Kosovo	Vojvodina	Slovenia	TOTAL
pupil	M	1				1				2
	F						1			1
scholar	M	1				3	5(1 lethal)			9
	F	1				5	2			8
soldiers	M	2	19							21
	F									
farmers	M	7		5		11(2 lethal)	7	1		31
	F									
housewife	M									
	F	5(2 lethal)	2	1		5(2 lethal)	5(1 lethal)			18
forest workers	M	14(3 lethal)				3(1 lethal)				17
	F	1								1
other	M	12	1			13(2 lethal)	1	1		28
	F	1				1				2
TOTAL	M	37(3 lethal)	20	5	ND	31(5 lethal)	13(1 lethal)	2	ND	108
	F	8(2 lethal)	2	1		11(2 lethal)	8(1 lethal)			30

ND=no data

Table 5

AGE OF SEROLOGICALLY COMFIRMED HFRS PATIENTS DURING EPIDEMIC IN 1989,IN YUGOSLAVIA

Locations / Age	Bosnia and Hercegovina	Croatia	Macedonia	Montenegro	Serbia	Kosovo	Vojvodina	Slovenia	TOTAL
0 -10					2	2			4
11-15	3				7	1/4			1/14
16-20	3	10			1	4			18
21-30	24	10	1		2/6	5	1		2/47
31-40	2/24	2	3		2/17	1	1		4/48
41-50	1/9		1		1/3	1/4			3/17
51-60	2/16	1			1/2	1			3/20
61-70	1/1					4			1/5
71-80	2				2				4
TOTAL	6/82	23	5	ND	6/40	2/25	2	ND	14/177
Serologically were comfirmed	108	27	6	1	43	29	2	10	226

No.died / No. with data of age

ND=No data

Figure 3. Seasonal distribution of HFRS cases in Yugoslavia during epidemic in 1989. Total number of cases (bold solid line), cases with Hantaan or Hantaan-like serotype (solid line), cases with Puumala serotype (broken line) and fatal cases (shaded areas) are shown.

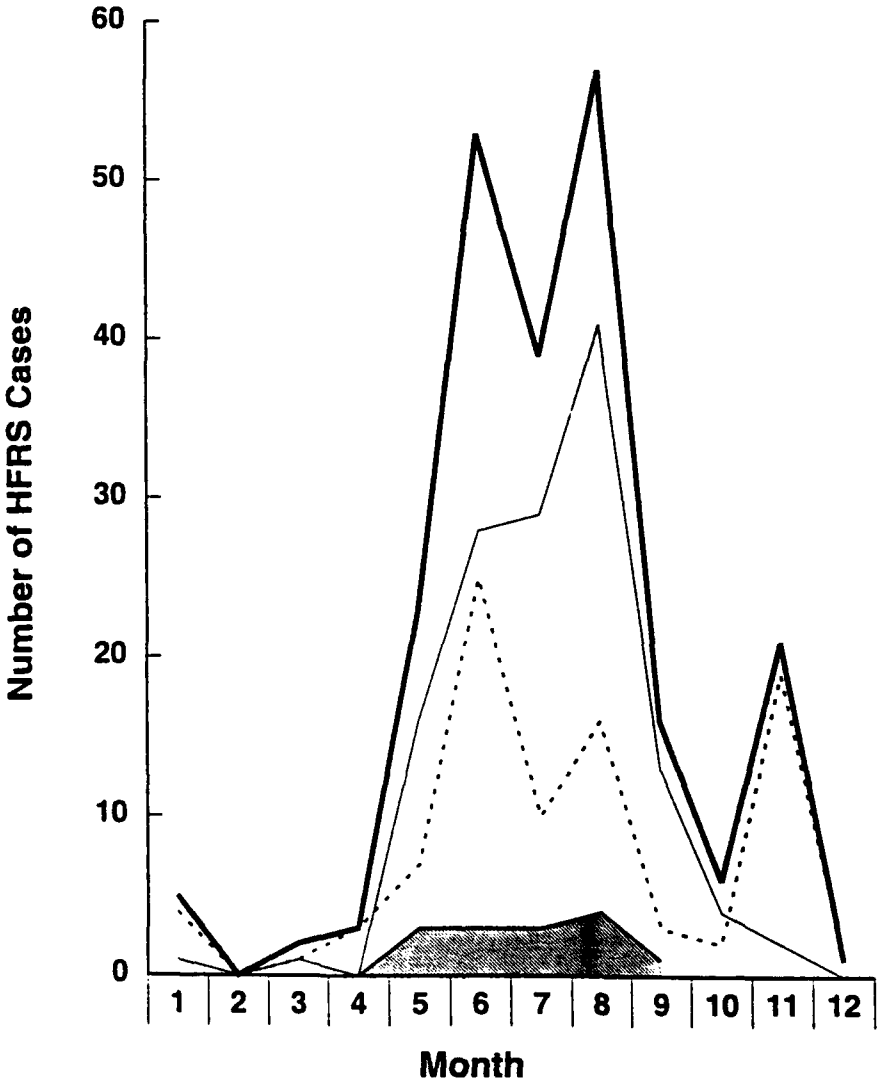

Table 6.

ANTIBODIES TO HANTAAN AND PUUMALA VIRUSES IN HEALTHY PERSONS FROM YUGOSLAVIA IN 1989.

Occupation of persons	No.sera tested	No. of positive			% positive	No.of HFRS cases
		HNT	Puumala	HNT + Puumala		
Residents of Oštarije place	193	10	-	-	5.2	3
Forest workers near Oštarije	45	-	-	1	2.2	-
Soldiers from all around Yugoslavia	201	5	6	1	5.9	223
T o t a l	439	15	6	2	5.2	226

Table 7.

ANTIBODIES TO HANTAAN AND PUUMALA VIRUSES IN HEALTHY RESIDENTS OF YUGOSLAVIA

Location	No.sera positive / No.sera treated	%	No. of HFRS cases
Ivanjica	45/84	54	>10
Požarevac	6/12	50	4
Foča	22/73	30,1	> 5
TOTAL	73/169		19

Table 8.

ANTIBODIES TO HANTAAN AND PUUMALA VIRUSES IN HEALTHY RESIDENTS OF OLOVO AND HADŽIĆI IN 1989.

Location	No.sera tested	No.sera positive			% positive	No.of HFRS cases
		HNT	Puumala	HNT + Puumala		
Olovo	78	8	3	5	20.5	> 30
Hadžići	75	14	3	1	24.0	> 40
T o t a l	153	22	6	6	22.2	> 80

Table 9.

Small mammals captured in endemic areas in Yugoslavia tested for IF antibodies to Hantaan and Puumala viruses and hantaviruses antigens

Location	Species	Number of Trapped	Number of Ang.Positive	Number of Ant.Positive	Numbe & Ant.P
Čačak	Apodemus flavicollis	1	1/1	0/1	
	A.sylvaticus	90	14/90	4/90	
	A.agrarius	44	6/44	2/44	
	A.microps	5	1/5	1/5	
	Sorex araneus	1	0/0	0/1	
	Crocidura subalveolens	8	2/8	0/2	
Ivanjica	A.flavicollis	12	3/12	2/12	
	A.sylvaticus	17	4/17	0/17	
	Clethrionomys glareolus	1	1/1	1/1	
	Pitimys subterraneus	1	1/1	0/1	
	Mus musculus	7	3/7	0/7	
	Sorex araneus	2	1/2	0/0	
	Neomys fodiens	2	2/2	0/0	
Požarevac	A.flavicollis	11	1/11	1/11	
	A.sylvaticus	24	5/24	2/24	
	A.agrarius	20	4/20	2/20	
	A.microps	1	0/1	0/0	
	P.subterraneus	2	0/2	0/0	
	M.arvalis	2	0/1	0/1	
	Mus musculus	21	8/20	6/18	
	Rattus norvegicus	5	5/5	4/5	
	Crocidura subalveolens	5	1/5	0/0	
Karlovac and Oštarije	A.flavicollis	1	1/1	0/1	
	A.sylvaticus	1	1/1	0/1	
	R.Norvegicus	16	4/16	7/16	
Novo Mesto	A.flavicollis	3	2/3	0/3	
	A.sylvaticus	6	1/6	0/6	
	P.subterraneus	1	0/1	0/1	
Plitvice Lakes	A.flavicollis	84	17/84	27/83	
	Cl.glareolus	60	18/60	30/58	1
	Sorex alpinus	1	1/1	0/1	
Olovo	A.flavicollis	28	7/28	12/25	
	A.sylvaticus	6	1/6	3/6	
	Mus musculus	1	1/1	1/1	
Hadžići	A.flavicollis	49	21/49	24/49	1
	A.sylvaticus	2	0/2	0/2	
	Cl.glareolus	2	1/2	0/2	
	M.species	1	0/1	0/1	
T O T A L		544	139/541	129/516	6

No.positive/No.examined

IF = imunofluorescent test; NT = not tested; Ang. = antigen; Ant. = antibody

Table 10.
Percentage of hantavirus antigen (IFA) in different species of small mammals according to different endemic foci of HFRS in Yugoslavia during epidemic in 1989

Endemic Foci	CACAK		IVANJICA		POZAREVAC		KARLOVAC		N. MESTO		PLITVICE		OLOVO		HADICI		TOTAL	
	%1	Ag+2	%1	Ag+2	%1	Ag+2	%1	Ag+2	%1	Ag+2	%1	Ag+2	%1	Ag+2	%1	Ag+2	%1	Ag+2
Small Mammals																		
APODEMUS AGRARIUS	29.5	15.9	-	-	22.2	20.0	-	-	-	-	-	-	-	-	-	-	11.8	17.2
A.FLAVICOLLIS	0.7	100.0	28.6	25.0	12.2	9.1	5.5	100.0	30.0	66.7	57.9	20.2	80.0	20.0	90.7	44.9	34.8	28.6
A.MICROPS	3.4	20.0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.9	20.0
A.SYLVATICUS	60.4	15.5	40.5	23.5	26.6	20.8	5.5	100.0	60.0	16.7	-	-	17.1	16.7	3.7	-	26.9	17.8
CLETHRIONOMYS GLAREOLUS	-	-	2.4	100.0	-	-	-	-	-	-	41.4	30.0	-	-	3.7	50.0	11.6	31.7
MICROTUS ARVALIS	-	-	-	-	2.2	-	-	-	-	-	-	-	-	-	-	-	0.4	-
MICROTUS SPECIES	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.8	-	0.2	-
PITIMYS SUB.	-	-	2.4	100.0	2.2	-	-	-	10.0	-	-	-	-	-	-	-	0.7	25.0
MUS MUSCULUS	-	-	16.6	42.8	23.3	40.0	-	-	-	-	-	-	2.8	100.0	-	-	5.3	32.1
RATTUS NORVEGICUS	-	-	-	-	5.5	100.0	88.9	25.0	-	-	-	-	-	-	-	-	3.9	42.8
CROCIDURA SUB	5.4	25.0	-	-	5.5	20.0	-	-	-	-	-	-	-	-	-	-	2.4	23.1
SOREX ALPINUS	-	-	-	-	-	-	-	-	-	-	0.7	100.0	-	-	-	-	0.2	100.0
SOREX ARANEUS	0.7	-	4.8	50.0	-	-	-	-	-	-	-	-	-	-	-	-	0.6	50.0
NEOMIS FODIENS	-	-	4.8	100.0	-	-	-	-	-	-	-	-	-	-	-	-	0.4	100.0
TOTAL No.	149	24	42	15	90	24	18	6	10	3	145	36	35	9	54	23	543	140
%	100.0	16.1		35.7		26.6		33.3		30.0		24.8		25.7		42.3		25.8

Ag = hantavirus antigen
"1" = % from the number of trapped small mammals
"2" = % Ag positive from total number of investigated species

TABLE 11.
Presence of hantavirus antigen and antibody in different species of small mammals according to age and sex during epidemic of HFRS in Yugoslavia in 1989

Mammals	Ag	Ab	Ag and Ab	Juvenile form	Subadult form	Adult form	Male	Female
APODEMUS AGRARIUS	11 / 64	6 / 64	6 / 64	3	36	25	31	33
A. FLAVICOLLIS	54 / 189	66 / 184	33 / 184	3	20	166	112	77
A. MICROPS	1 / 4	1 / 4	1 / 4	0	1	4	1	4
A. SYLVATICUS	26 / 146	9 / 146	6 / 146	3	31	112	89	57
CL. GLAREOLUS	20 / 63	31 / 61	15 / 61	0	3	60	18	45
MICROTUS ARVALIS	0 / 1	0 / 1	0 / 1	0	1	1	2	0
MICROTUS SPECIES	0 / 1	0 / 1	0 / 1	0	0	1	1	0
PITIMYS SUB.	1 / 4	0 / 2	0 / 2	0	1	3	0	4
MUS MUSCULUS	9 / 29	5 / 26	5 / 26	4	7	18	15	14
RATTUS NORVEGICUS	9 / 21	11 / 21	6 / 21	6	0	15	8	13
CROCIDURA SUB.	3 / 13	0 / 2	0 / 2	0	2	11	7	6
SOREX ALPINUS	1 / 1	0 / 1	0 / 1	0	0	1	1	0
SOREX ARANEUS	1 / 2	0 / 1	0 / 1	0	1	2	1	2
NEOMIS FODIENS	2 / 2	0 / 0	0 / 0	0	0	2	1	1
TOTAL	139/540	129/516	67/516	19	103	421	287	256

Ag+ = No. hantavirus antigen positive / No of investigated
Ab+ = No. hantavirus antibody positive / No of investigated

TABLE 12.
Percentage of hantavirus antigen and antibody positive small mammals according age and sex in correlation with different focci of HFRS in Yugoslavia in 1989

FOCI	CACAK	IVANJICA	POZAREVAC	KARLOVAC	NOVO MESTO	PLITVICE	OLOVO	HADICI	TOTAL
Ag+	16.2	35.7	26.6	33.3	30.0	24.8	25.7	42.6	25.8
Ab+	4.9	7.9	16.6	38.8	0.0	40.1	50.0	44.4	25.0
Ag+ and Ab+	4.2	5.2	15.4	11.1	0.0	16.2	21.8	27.7	12.9
Juvenile	2.1	0.0	6.6	33.3	10.0	1.4	0.0	1.8	3.5
Subadult	40.9	4.7	22.2	0.0	10.0	13.8	5.7	1.9	18.9
Adult	55.7	95.3	71.2	66.7	80.0	84.8	94.3	96.3	77.6
Male	63.7	33.3	46.7	44.4	60.0	44.8	71.4	66.7	52.8
Female	36.3	66.7	53.3	55.6	40.0	55.2	28.6	33.3	47.2

Ag+ = No. of Antigen positive
Ab+ = No. of Antibody positive

TABLE 13.
Hantavirus antigen and antibody positive small mammals in CACAK region according to age and sex

CAKAK	No.trapped	Ag+	Ab+	Ag+andAb+	Juvenile form	Subadult form	Adult form	Male	Female
APODEMUS AGRARIUS	44	7	2	2	1	27	16	22	22
A.FLAVICOLLIS	1	0	0	0	0	0	1	1	0
A.MICROPS	5	1	1	1	0	1	4	1	4
A.SYLVATICUS	90	14	4	4	2	26	62	67	23
CROCIDURA SPEC.	8	2	0	0	0	6	2	4	4
SOREX ARANEUS	1	0	0	0	0	0	1	1	0
TOTAL No.	149	24	7	7	3	60	86	96	53

Ag+ = No. of Antigen positive
Ab+ = No. of Antibody positive

TABLE 14.
Hantavirus antigen and antibody positive small mammals in IVANJICA region according to age and sex

IVANJICA	No.trapped	Ag+	Ab+	Ag+ and Ab+	Juvenile form	Subadult form	Adult form	Male	Female
APODEMUS FLAVICOLLIS	12	3	2	1	0	0	12	4	8
A.SYLVATICUS	17	4	0	0	0	1	16	6	11
CL.GLAREOLUS	1	1	1	1	0	0	1	0	1
PITIMYS SUBTERRANEUS	1	1	0	0	0	0	1	0	1
MUS MUSCULUS	7	3	0	0	0	0	7	3	4
SOREX ARANEUS	2	1	0	0	0	1	1	0	2
NEOMIS FODIENS	2	2	0	0	0	0	2	1	1
TOTAL No.	42	15	3	2	0	2	40	14	28

Ag+ = No. of Antigen positive
Ab+ = No. of Antibody positive

TABLE 15.
Hantavirus antigen and antibody positive small mammals in POZAREVAC region according to age and sex

POZAREVAC	No.trapped	Ag +	Ab+	Ag+ and Ab+	Juvenile form	Subadult form	Adult form	Male	Female
APODEMUS AGRARIUS	20	4	2	2	2	8	10	9	11
A.FLAVICOLLIS	11	1	1	1	0	1	10	6	5
A.MICROPS	1	0	0	0	0	0	1	0	1
A.SYLVATICUS	24	5	2	1	0	2	22	9	15
MICROTUS ARVALIS	2	0	0	0	0	1	1	2	0
PITIMYS SUBTERRANEUS	2	0	0	0	0	1	1	0	2
MUS MUSCULUS	21	8	4	4	4	7	10	11	10
RATTUS NORVEGICUS	5	5	4	4	0	0	5	2	3
CROCIDURA SUB.	5	1	0	0	0	0	5	3	2
TOTAL No.	91	24	13	12	6	20	65	42	49

Ag+ = No. of Antigen positive
Ab+ = No. of Antibody positive

TABLE 16.
Hantavirus antigen and antibody positive small mammals in KARLOVAC region according to age and sex

KARLOVAC	No,trapped	Ag+	Ab+	Ag+andAb+	Juvenile form	Subadult form	Adult form	Male	Female
APODEMUS FLAVICOLLIS	1	1	0	0	0	0	1	1	0
A.SYLVATICUS	1	1	0	0	0	0	1	1	0
RATTUS NORVEGICUS	16	4	7	2	6	0	10	6	10
TOTAL No.	18	6	7	2	6	0	12	8	10

Ag+ = No.of Antigen positive
Ab+ = No .of Antibody positive

TABLE 17.
Hantavirus antigen and antibody positive small mammals in NOVO MESTO region according to age and sex

NOVO MESTO	No,trapped	Ag+	Ab+	Ag+ and Ab+	Juvenile form	Subadult form	Adult form	Male	Female
APODEMUS SYLVATICUS	6	1	0	0	1	1	4	4	2
PITIMYS SUBTERRANEUS	1	0	0	0	0	0	1	0	1
RATTUS NORVEGICUS	3	2	0	0	0	0	3	2	1
TOTAL No.	10	3	0	0	1	1	8	6	4

Ag+ = No. of Antigen positive
Ab+ = No. of Antibody positive

TABLE 18.
Hantavirus antigen and antibody positive small mammals in PLITVICE region according to age and sex

PLITVICE	No.trapped	Ag+	Ab+	Ag+andAb+	Juvenile form	Subadult form	Adult form	Male	Female
APODEMUS FLAVICOLLIS	84	17	27	9	2	17	65	47	37
CI.GLAREOLUS	60	18	30	14	0	3	57	18	42
SOREX ALPINUS	1	1	0	0	0	0	1	0	1
TOTAL No.	145	36	57	23	2	20	123	65	80

Ag+ = No. of Antigen positive
Ab+ = No. of Antibody positive

TABLE 19.
Hantavirus antigen and antibody positive small mammals in OLOVO region according to age and sex

OLOVO	No.trapped	Ag+	Ab+	Ag+ and Ab+	Juvenile form	Subadult form	Adult form	Male	Female
APODEMUS FLAVICOLLIS	28	7	12	5	0	2	26	22	6
A.SYLVATICUS	6	1	3	1	0	0	6	2	4
MUS MUSCULUS	1	1	1	1	0	0	1	1	0
TOTAL No.	35	9	16	7	0	2	33	25	10

Ag+ = No. of Antigen positive
Ab+ = No. of Antibody positive

TABLE 20.

Hantavirus antigen and antibody positive small mammals in HADICI rergion according to age and sex

HADICI	No,trapped	Ag+	Ab+	Ag+ and Ab+	Juvenile form	Subadult form	Adult form	Male	Female
APODEMUS FLAVICOLLIS	49	22	24	15	1	0	48	35	14
A.SYLVATICUS	2	0	0	0	0	1	1	0	2
CI.GLAREOLUS	2	1	0	0	0	0	2	0	2
MICROTUS SPECIES	1	0	0	0	0	0	1	1	0
TOTAL No.	54	23	24	15	1	1	52	36	18

Ag+ = No. of Antigen positive
Ab+ = No. of Antibody positive

TABLE 21.
Percentage of hantavirus antigen and antibody positive
APODEMUS FLAVICOLLIS by age and sex in different foci of HFRS in 1989

APODEMUS FLAVICOLLIS	CACAK	IVANJICA	POZAREVAC	KARLOVAC	NOVOMESTO	PLITVICE	OLOVO	HADICI	TOTAL
No. trapped	1	12	11	1	3	84	28	49	189
%	0.7	28.6	12.2	5.5	30.0	57.9	80.0	90.7	33.8
%Ag+	100.0	25.0	9.1	100.0	66.7	20.2	25.0	44.4	28.6
%Ab+	0.0	16.7	9.1	0.0	0.0	32.5	48.0	48.9	35.9
%Ag+ and Ab+	0.0	8.3	9.1	0.0	0.0	10.7	17.8	30.6	17.9
% Juvenile	0.0	0.0	0.0	0.0	0.0	2.4	0.0	2.1	1.6
% Subadult	0.0	0.0	9.1	0.0	0.0	20.2	7.1	0.0	10.5
% Adult	100.0	100.0	90.9	100.0	100.0	77.4	92.9	97.9	87.9
Male	100.0	35.0	54.5	100.0	66.6	55.9	78.6	71.4	58.9
Female	0.0	65.0	45.5	0.0	33.3	44.1	21.4	28.6	41.1

Ag+ = Antigen positive
Ab+ = Antibody positive

TABLE 22.
Percentage of hantavirus antigen and antibody positive
APODEMUS SYLVATICUS by age and sex in different foci of HFRS in 1989

APODEMUS SYLVATICUS	CACAK	IVANJICA	POZAREVAC	KARLOVAC	NOVO MESTO	PLITVICE	OLOVO	HADICI	TOTAL
No,trapped	90	17	24	1	6	0	6	2	146
%	60.4	40.5	26.7	6.3	60.0	0.0	17.1	3.7	26.9
%Ag+	15.5	23.5	20.8	100.0	16.7	0.0	16.7	0.0	17.8
%Ab+	4.4	0.0	8.3	0.0	0.0	0.0	50.0	0.0	6.2
%Ag+ and Ab+	4.4	0.0	4.2	0.0	0.0	0.0	16.7	0.0	4.1
% Juvenile	2.2	0.0	0.0	0.0	16.7	0.0	0.0	0.0	2.1
% Subadult	28.8	5.9	8.3	0.0	16.7	0.0	0.0	50.0	21.2
% Adult	69.0	94.1	91.7	100.0	66.6	0.0	100.0	50.0	76.7
Male	34.4	35.3	37.5	100.0	66.6	0.0	33.4	0.0	60.9
Female	25.6	64.7	62.5	0.0	33.4	0.0	66.6	100.0	39.1

Ag+ = Antigen positive
Ab+ = Antibody positive

TABLE 23.
Percentage of hantavirus antigen and antibody positive
APODEMUS AGRARIUS by age and sex in different foci of HFRS in 1989

APODEMUS AGRARIUS	CACAK	IVANJICA	POZAREVAC	KARLOVAC	NOVO MESTO	PLITVICE	OLOVO	HADICI	TOTAL
No,trapped	44	0	20	0	0	0	0	0	64
%	29.5	0.0	22.2	0.0	0.0	0.0	0.0	0.0	11.8
% Ag+	15.9	0.0	20.0	0.0	0.0	0.0	0.0	0.0	17.2
% Ab+	4.5	0.0	10.0	0.0	0.0	0.0	0.0	0.0	9.4
% Ag+ and Ab+	4.5	0.0	10.0	0.0	0.0	0.0	0.0	0.0	9.4
% Juvenile	2.3	0.0	10.0	0.0	0.0	0.0	0.0	0.0	4.7
% Subadult	61.4	0.0	40.0	0.0	0.0	0.0	0.0	0.0	56.2
% Adult	36.3	0.0	50.0	0.0	0.0	0.0	0.0	0.0	39.1
Male	50.0	0.0	45.0	0.0	0.0	0.0	0.0	0.0	48.4
Female	50.0	0.0	55.0	0.0	0.0	0.0	0.0	0.0	51.6

Ag+ = Antigen positive
Ab+ = Antibody positive

TABLE 24.
Percentage of hantavirus antigen and antibody positive
CLETHRIONOMYS GLAREOLUS by age and sex in different foci of HFRS in 1989

CLETHRIONOMYS GLAREOLUS	CACAK	IVANJICA	POZAREVAC	KARLOVAC	NOVO MESTO	PLITVICE	OLOVO	HADICI	TOTAL
No.trapped	0	1	0	0	0	60	0	2	63
%	0.0	2.4	0.0	0.0	0.0	41.2	0.0	4.1	11.6
% Ag+	0.0	100.0	0.0	0.0	0.0	30.0	0.0	50.0	31.7
% Ab+	0.0	100.0	0.0	0.0	0.0	51.7	0.0	0.0	50.8
% Ag+ and Ab+	0.0	100.0	0.0	0.0	0.0	24.1	0.0	0.0	24.6
% Juvenile	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
% Subadult	0.0	0.0	0.0	0.0	0.0	5.0	0.0	50.0	4.8
% Adult	0.0	100.0	0.0	0.0	0.0	95.0	0.0	50.0	95.2
Male	0.0	0.0	0.0	0.0	0.0	30.0	0.0	0.0	28.6
Female	0.0	100.0	0.0	0.0	0.0	70.0	0.0	100.0	71.4

Ag+ = Antigen positive
Ab+ = Antibody positive

TABLE 25.
Percentage hantavirus antigen and antibody positive
MUS MUSCULUS by age and sex in different foci of HFRS in 1989

MUS MUSCULUS	CACAK	IVANJICA	POZAREVAC	KARLOVAC	NOVO MESTO	PLITVICE	OLOVO	HADICI	TOTAL
No.trapped	0	0	21	0	0	0	1	0	22
%	0	0	23.3	0	0	0	2.8	0	4.1
% Ag+	0	0	40.0	0	0	0	100.0	0	32.1
%Ab+	0	0	22.2	0	0	0	100.0	0	19.2
% Ag+ and Ab+	0	0	22.2	0	0	0	100.0	0	19.2
% Juvenile	0	0	19.1	0	0	0	0.0	0	18.2
% Subadult	0	0	33.3	0	0	0	0.0	0	31.8
% Adult	0	0	47.6	0	0	0	100.0	0	50.0
Male	0	0	52.4	0	0	0	100.0	0	50.0
Female	0	0	47.6	0	0	0	0.0	0	50.0

Ag+ = Antigen positive
Ab+ = Antibody positive

TABLE 26.
Percentage hantavirus antigen and antibody positive
RATTUS NORVEGICUS by age and sex in different foci of HFRS in 1989

RATTUS NORVEGICUS	CACAK	IVANJICA	POZAREVAC	KARLOVAC	NOVO MESTO	PLITVICE	OLOVO	HADICI	TOTAL
No trapped	0	0	5	16	0	0	0	0	21
%	0	0	5.5	88.9	0	0	0	0	3.9
%Ag+	0	0	100.0	25.0	0	0	0	0	42.8
%Ab+	0	0	80.0	43.7	0	0	0	0	52.4
% Ag+ and Ab+	0	0	80.0	12.5	0	0	0	0	28.6
% Juvenile	0	0	0.0	37.5	0	0	0	0	28.6
% Subadult	0	0	0.0	0.0	0	0	0	0	0.0
% Adult	0	0	100.0	62.5	0	0	0	0	71.4
Male	0	0	40.0	37.5	0	0	0	0	38.1
Female	0	0	60.0	62.5	0	0	0	0	61.9

Ag+ = Antigen positive
Ab+ = Antibody positive

TABLE 27.
Percentage hantavirus antigen and antibody positive
CROCIDURA SPECIES by age and sex in different foci OF HFRS in 1989

CROCIDURA SPECIES	CACAK	IVANJICA	POZAREVAC	KARLOVAC	NOVO MESTO	PLITVICE	OLOVO	HADICI	TOTAL
No trapped	8	0	5	0	0	0	0	0	13
%	5.4	0	5.5	0	0	0	0	0	2.4
% Ag+	25.0	0	20.0	0	0	0	0	0	23.1
%Ab+	0.0	0	0.0	0	0	0	0	0	0.0
% Ag+ and Ab+	0.0	0	0.0	0	0	0	0	0	0.0
% Juvenile	0.0	0	0.0	0	0	0	0	0	0.0
% Subadult	75.0	0	0.0	0	0	0	0	0	15.4
% Adult	25.0	0	100.0	0	0	0	0	0	84.6
Male	50.0	0	60.0	0	0	0	0	0	53.8
Female	50.0	0	40.0	0	0	0	0	0	46.2

Ag+ = Antigen positive
Ab+ = Antibody positive

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1
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